IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Docket No: Q76937
Ryuji UENO

Appln. No.: 10/567,462 Group Art Unit: 1627
Confirmation No.: 1105 Examiner: Kendra D. Carter
Filed: February 5, 2007

For: COMPOSITION AND METHOD FOR PROMOTING HAIR GROWTH

DECLARATION UNDER RULE 1.132

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, TABUCHI, Reiko, a citizen of Japan and residing in Kawanishi-shi, Hyogo, Japan declare and say as follows:

1. I graduated from Department of Pharmacy, School of Pharmaceutical Science, Mukogawa Women's University, Hyogo Japan in March 1981 and hold a bachelor's degree in pharmacology.

2. From April 1981 to March 2003, I was an employee of UENO FINE CHEMICALS INDUSTRY, LTD of Osaka, Japan and engaged in the research and development in the field of pharmacology and toxicology. Since April 2003 up to this time, I have been an employee of R-TECH UENO, LTD of Tokyo, Japan.

3. At present, I am a member of The Japanese Society of Toxicology.

4. I am familiar with the subject matter of the above-identified application.

5. I have read the Office Action mailed April 21, 2011 and the references cited therein and am familiar with the

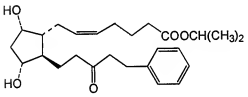
subject matter thereof.

6. In order to show that the invention claimed in the above-identified application is unobvious over Johnstone (US6,262,105) in view of Skuballa et al. (US 4,088,775), the following experiments have been done.

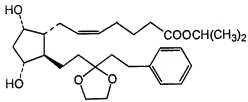
EXPERIMENTS

1. **Test Method**

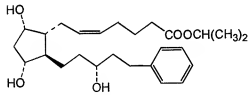
Test compound A: 13,14-dihydro-15-keto-17-phenyl-18,19,20-trinor-$PGF_{2\alpha}$ isopropyl ester



Test compound B: 13,14-dihydro-15,15-ethylenedioxy-17-phenyl-18,19,20-trinor-$PGF_{2\alpha}$ isopropyl ester



Latanoprost: 13,14-dihydro-17-phenyl-18,19,20-trinor $PGF_{2\alpha}$ isopropyl ester



Each test compounds were dissolved in 70% (w/w) aqueous ethanol. Each dose formulation of test compound was evenly applied topically once daily (100 mL per mouse) to the clipped dorsal skin area (approximately 2 x 4 cm), except for Saturday and Sunday, for 30 days. The control group received an equal amount

of the vehicle in the same manner.

Table 1. Effects of Topical Application of Compound A and Latanoprost on Hair Growth in C3H/HeN Mice

Groups	Animal No.	Hair Growth Score Days of Treatments							
		19	22	23	24	25	26	29	30
Control (Vehicle)	11	-	-	-	-	-	-	-	-
	12	-	-	-	-	-	-	-	-
	13	-	-	-	-	-	-	-	-
Compound A 0.005%	21	-	-	-	-	-	-	-	-
	22	-	-	-	-	-	-	-	-
	23	-	-	-	-	-	-	-	-
Compound A 0.01%	31	-	-	-	-	-	-	-	-
	32	-	-	-	-	-	-	-	-
	33	-	-	-	-	-	-	-	-
Compound A 0.03%	31	-	-	-	-	-	-	-	-
	32	-	-	-	-	-	-	-	-
	33	-	-	-	-	-	-	-	-
Latanoprost 0.005%	51	-	±	+	+	++	++	++	+++
	52	-	-	±	±	±	±	+	++
	53	±	±	±	±	+	++	++	++
Latanoprost 0.01%	61	-	-	±	+	+	+	++	++
	62	-	-	-	±	±	±	+	++
	63	-	-	±	±	±	±	+	+
Latanoprost 0.03%	71	-	±	±	±	±	±	+	++
	72	-	-	±	±	±	+	+	+
	73	-	±	±	+	+	+	++	++

- no hair growth observed
± hair growth less than 10% of clipped area
\+ hair growth 10 - 30% of clipped area
++ hair growth 30 - 50% of clipped area
+++ hair growth more than 50% of clipped area

Table 2. Effects of Topical Application of Compound B and Latanoprost on Hair Growth in C3H/HeN Mice

Groups	Animal No.	Hair Growth Score Days of Treatments							
		14	16	18	21	23	25	28	30
Control (Vehicle)	0101	-	-	-	-	-	-	-	-
	0102	-	-	-	-	-	-	-	-
	0103	-	-	-	-	-	-	-	-
Compound B 0.01%	0401	-	-	±	±	+	+	++	++
	0402	-	-	±	+	++	+++	+++	+++
	0403	-	-	-	-	±	±	++	+++
Compound B 0.1%	0501	-	-	±	±	+	++	++	++
	0502	-	-	-	±	+	+	++	+++
	0503	-	-	-	±	+	++	++	+++
Latanoprost 0.005%	1201	-	-	±	+	+	++	+++	+++
	1202	-	-	-	±	+	+	++	++
	1203	-	-	-	±	±	+	+	++

- no hair growth observed
± hair growth less than 10% of clipped area
\+ hair growth 10 - 40% of clipped area
++ hair growth 40 - 80% of clipped area
+++ hair growth more than 80% of clipped area

I consider that if one were to combine Johnstone with Skuballa, one would first change the 15-OH of latanoprost (the compound used in Johnstone's working examples) to 15-ketal, and then when one would see that the latanoprost modified to include 15-ketal has a weaker effect than latanoprost itself (note the results for latanoprost are based on latanoprost used at 0.005%), one would not have been motivated to modify Johnstone to arrive at the present invention. Indeed, the evidence set forth above shows that even substituting 15-keto, which is disclosed in Johnstone itself, in place of 15-OH of latanoprost is not effective, so this is another reason why one would not have been motivated to substitute 15-ketal, which is not even disclosed in Johnstone, into Johnstone's compound.

In view of the evidence set forth above and the evidence of record, I conclude that the present invention provides unexpectedly superior results.

7. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified application or any patent issuing thereon.

Dated this 20 day of July, 2011

R. Tabuchi

Reiko TABUCHI